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Pesticide Fact Sheet Number 28: Linuron

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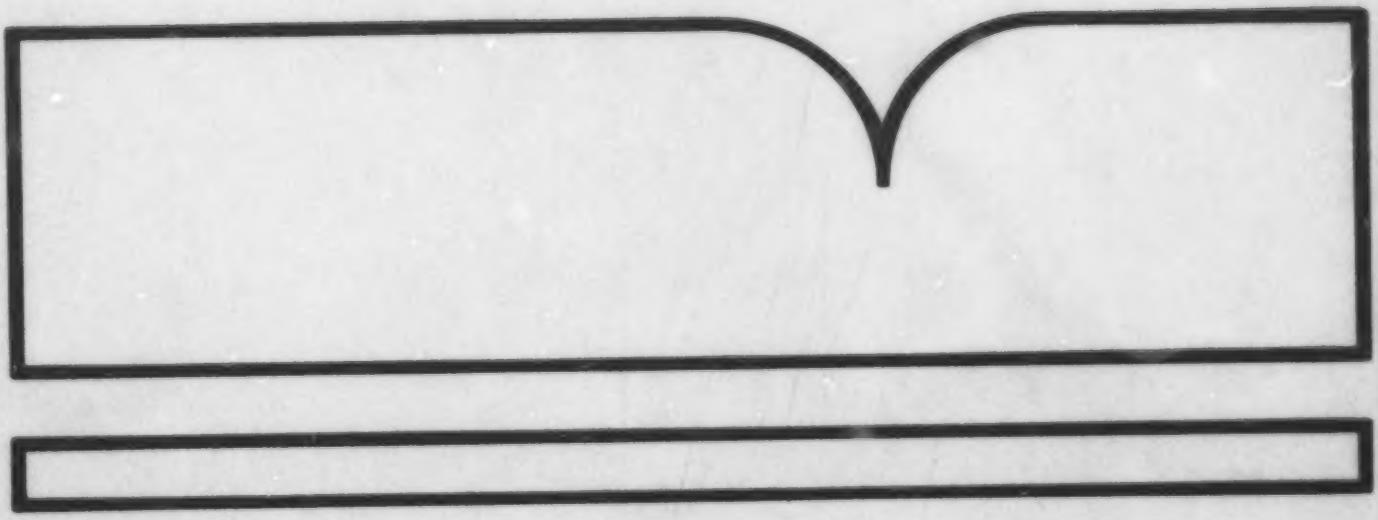

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16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

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b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

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Office of Pesticides and Toxic Substances
Office of Pesticide Programs (TS-788C)
Washington, DC 20460

EPA

Pesticide Fact Sheet

Name of Chemical: LINURON
Reason for Issuance:
Date Issued: June 30, 1984
Fact Sheet Number: 28

1. Description of the chemical:

Generic name: 3-(3,4-Dichlorophenyl)-1-methoxy-1-methylurea ($C_9H_{10}Cl_2N_2O_2$)
Common name: Linuron
Trade name: Alfanox®, Linurex®, Londax®. Lorox®
EPA Shaughnessy Code: 035506
Chemical Abstracts Service (CAS) Registry number: 330-55-2
Year of initial registration: 1966
Pesticide Type: Herbicide
Chemical family: Substituted urea
U.S. and foreign producers: E. I. duPont de Nemours and Company, Drexel Chemical Company, Griffin Corporation, Vertac Chemical Corp., Bayer AG, Makhteshim-Agan, Pennwalt Holland B. V., Rhone-Poulenc, Staveley Chemicals Ltd., and Universal Crop Protection Ltd.

2. Use patterns and formulations:

Application sites: Linuron is a substituted urea compound registered for use as a herbicide to control a wide variety of annual and perennial broadleaf and grassy weeds on both crop and noncrop sites. Linuron is registered for use on numerous crop sites such as forage crops, field crops, fruits, vegetable, and ornamental crops. In noncrop applications, linuron is used on alleys, fencerows, fairways, highway right-of-way, sodfields, streets, and vacant lots.

Types of formulations: Linuron is available as a wettable powder, granular flowable, and liquid suspensions.

Types and methods of applications: Linuron is applied as follows: broadcast or band upon the soil surface using ground or aerial equipment.

Application rates: 0.5 lbs. a.i./A to 3.0 lbs. a.i./A on crop sites; and 1.0 lbs. a.i./A to 3.0 lbs. a.i./A on noncrop sites.

Usual carriers: Water, oil and clay.

3. Science Findings:

Summary science statements:

Linuron has low acute mammalian toxicity and it's uses are not expected to adversely affect avian and mammalian wildlife. The metabolism of linuron in plants and animals is adequately understood.

Dietary exposures to linuron have induced dose related tumors in the rat testes and mouse liver. The available toxicology data are insufficient to fully assess the longterm reproductive and teratogenic potential of linuron.

Chemical characteristics:

Technical linuron is an odorless, white, crystalline solid. It is stable towards oxidation and moisture under conventional conditions and decomposes at 180-190°C. The chemical does not exhibit any unusual handling hazards.

Toxicological characteristics:

Acute toxicology studies on linuron are as follows:
Oral LD_{50} in rats: 1,500 mg/kg body weight, Toxicity Category III
Dermal LD_{50} in rats: > 2,000 mg/kg body weight, Toxicity Category III
Inhalation LC_{50} in rats: 218 mg/l/hr, Toxicity Category IV
Skin irritation in rabbits: slight irritant, Toxicity Category III
Eye irritation in rabbits: slight irritant, Toxicity Category III.

Chronic toxicology studies on linuron are as follows:
A two year chronic feeding study on rats has shown that interstitial testicular (ISC) adenomas occured in all dosage groups(control, 50.0, 125.0, and 625.0 ppm) both during the two years and then at term.

A chronic feeding study was conducted on male and female mice at diet levels of 0.0, 50.0, 150.0, and 1,500 ppm of linuron. The study showed a statistically significant increase of hepatocellular adenomas in the female mice from the highest dose group (1,500 ppm). A significant increase of hepatocellular adenomas was also observed among the males in the lowest dose group (50 ppm). The levels of methemoglobin were increased in treated mice of both sexes; this increase was related to the linuron administration.

A two year dog study did not demonstrate carcinogenesis but showed hemosiderin deposition at 125 and 625 ppm.

In several mutagenicity tests, Linuron did not affect DNA repair but may have inhibited mouse testicular DNA synthesis. Linuron has not been shown to be active in the Ames test. Linuron did not affect S. typhimurium in vivo in the mouse peritoneal cavity.

Major routes of human exposure:

The non-dietary exposure to linuron by a farmer as an applicator or *mixer/loader is very high.*

The dietary exposure to linuron residues by the U.S. population is probable because of its consumption of treated crops.

Physiological and Biochemical Behavioral Characteristics:

Absorption characteristics: Linuron is most readily absorbed through the root system; less through foliage and stems.
Translocation: Linuron is translocated upward primarily in the xylem.
Mechanism of pesticidal action: It is a strong inhibitor of photosynthesis (Hill reaction).

Environmental characteristics:

Adsorption and leaching in basic soil types: Adsorption increases as clay content and/or organic matter content of soil increases; clays of high exchange capacity absorb more linuron than those of low exchange capacity.

Microbial breakdown: microbes are the primary factor in the breakdown of linuron in soils.

The available environmental fate data are insufficient to fully assess the degradation, metabolism, mobility, dissipation and accumulation activities of linuron. When additional studies are submitted, a complete environmental assessment can be made.

Ecological characteristics:

Avian LC_{50}: >3,000 mg/kg,
Fish LC_{50}: (96 hour), 16 ppm for bluegill and rainbow trout,
LC_{50}: (72 hour) >40 ppm for crawfish,
LC_{50}: (48 hour) >40 ppm for tadpole.

When additional ecological effects data are submitted, a complete hazard assessment can be made.

Tolerance assessments:

Since linuron and diuron have certain metabolites in common [1-(3,4-dichlorophenyl)-3-methylurea (DCPMU), and 3,4-dichlorophenylurea (DCPU)], the Agency will consider diuron's residue contribution in the tolerance reassessment of linuron for the following commodities: corn, sorghum, grains, wheat, asparagus, meat(red), and cottonseed.

If the complete tolerance reassessments for the above commodities are favorable, tolerances for residues of linuron and metabolites (which will hydrolyze to form 3,4-dichloroaniline) will have to be proposed for residues in milk and eggs at 0.05 ppm.

The tolerances listed below have not been revised:

Commodities	Parts per million
Asparagus	3.0
Carrots	1.0
Cattle, fat	1.0
Cattle, meat by-products	1.0
Cattle, meat	1.0
Celery	1.0
Corn, field, fodder	1.0
Corn, field, forage	1.0
Corn, fresh, (sweet)	0.25
Corn, grain (inc. pop)	0.25
Corn, pop, fodder	1.0
Corn, pop, forage	1.0
Corn, sweet, fodder	1.0
Corn, sweet, forage	0.25
Goats, fat	1.0
Goats, meat by-products	1.0
Goats, meat	1.0
Hogs, fat	1.0
Hogs, meat by-products	1.0
Hogs, meat	1.0
Horses, fat	1.0
Horses, meat by-products	1.0
Horses, meat	1.0
Parsnips (with or without tops)	0.5
Parsnips, tops	0.5
Potatoes	1.0
Sheep, fat	1.0
Sheep, meat by-products	1.0
Sheep, meat	1.0
Sorghum, fodder	1.0
Sorghum, forage	1.0
Sorghum, grain(milo)	0.25
Soybeans (dry or succulent)	1.0
Soybeans, forage	1.0
Soybeans, hay	1.0
Wheat, forage	0.5
Wheat, grain	0.25
Wheat, hay	0.5
Wheat, straw	0.5

Problems known to have occurred with use:

Exposure of humans to linuron through runoff contamination of surface water after heavy Spring precipitation has occurred in Northwestern Ohio.

4. Summary of regulatory position and rationale:

Use classification

Restricted use classification.

Unique label warning statements:

"The use of this product may be hazardous to your health. This product contains linuron, which has been determined to cause tumors in laboratory animals."

"Do not reenter treated areas for 24 hours following application unless protective clothing is worn."

Summary of risk/benefit review:

The Agency has determined that linuron has exceeded the oncogenicity risk criteria and requires special review. Dietary exposure to linuron indicated clear evidence of oncogenicity for male rats using the NTP criteria. Using these data, the Agency calculated nondietary risk. The most realistic scenario is a farmer with no protection, who mixes/loads and applies this herbicide. This calculation resulted in a risk of 3.6×10^{-4} to 2.2×10^{-3}. It is possible that the actual risk may even be higher, because the commercial applicator exposure was not included. The Agency also calculated dietary risk. The most realistic scenario for dietary risk is the combination of maximum residue expected (MRE) and percent crop which resulted in a risk of 1.5×10^{-5}.

5. Summary of major data gaps:

The following toxicology data are required:

Two teratology studies, one in rat and one in another species (rabbit). A two-generation reproduction study in rats is required; this study must be designed to incorporate concerns regarding the significance of interstitial cell adenomas. Note that in the former studies (rat and dog), reticulocytes and erythroid precursors were not measured. This is a data gap, since at the high dose level (625 ppm), hemosiderin was observed in rats and also at 125 and 625 ppm in the dog. (This data may be filled by appropriate design inclusion into the required reproduction study above. The registrant must consult with the Agency on the appropriate protocol.)

Mutagenicity* and related data are required, which (1) satisfy the 3 mutagenicity testing category requirements, (2) adequately identify the risks, and where possible identify the mechanisms associated with positive findings in rodent chronic studies. The Agency is requiring data, relating levels of sulf- and methemoglobin following dietary exposure for certain substituted phenyl urea compounds such as linuron. This testing may be combined with other testing involving dietary exposure, such as the reproduction study. Dose levels must be such that a NOEL may be established.

The following four mutagenicity studies* have been received and are in Agency review:

1. "Mutagencity Evaluation In (Salmonella typhimurium)", HLR 1006-83, 5/5/83,
2. "Unscheduled DNA Synthesis/Rat Hepatocytes In Vitro", HLR 190-83, 6/3/83,
3. "CHO/HGPRT Assay for Gene Mutation", HLR 540-83, 12/16/83,
4. "In Vivo Bone Marrow Chromosome Study in Rats", HLO 378-83, 9/1/83.

The available toxicology data are insufficient to fully assess the long-term reproductive, and teratogenic potential of linuron. Long-term studies must be submitted from one to two years after receipt of the guidance package. Please refer to the toxicology data tables under § 158.135 for the specific dates for which long term data must be submitted. Short-term studies must be submitted within six months after receipt of this guidance package.

The following environmental fate data are required:

Hydrolysis test,
Photodegradation test in water,
Photodegradation test in soil,
Photodegradation test in air,
Metabolism test in aerobic soil
Metabolism test in anaerobic soil,
Leaching and adsosrption/desorption,
Mobility (volatility) test in the lab,
Mobility (volatility) test in the field,
Dissipation study in soil,
Dissipation study in soil (long tterm),
Accumulation study in fish,
Special Testing on applicator exposure,
Reentry data requirements.

Long-term studies must be submitted from one to four years after receipt of the guidance package. Please refer to the environmental fate data tables under § 158.130 for the specific dates for which long term data must be submitted. Short-term studies must be submitted within six months after receipt of the guidance package.

The following ecological effects data are required:

Acute avian toxicity,
Acute toxicity, freshwater fish,
Acute toxicity, freshwater invertebrates.

Acute studies must be submitted within six months after receipt of this guidance package.

The physical/chemical requirements listed in the §158.120, Product Chemistry data tables must be submitted, particularly:

Solubility,
Vapor pressure,
Octanol/water partition coefficient.

These studies must be submitted within six months after receipt of this guidance package.

The following residue data are required:

Residue data for asparagus, carrots, celery, corn, cottonseed, parsnips, potatoes, sorghum,, soybeans, and wheat are required to reflect uses of the 50%, dry flowable (DF) and 4 lb/gal, flowable concentrate (FIC) formulations. Data reflecting uses of the 50% DF are required for the following commodities: carrots (aerial applications), potatoes (aerial applications), soybeans (preemergence), sorghum (forage), wheat (forage and hay), asparagus (preemergence), and cottonseed (two applications per season). Data pertaining to residues in dehydrated potato products are required.

Long-term studies must be submitted within one year after receipt of this guidance package.

6. Contact Person at EPA:

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